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CENTRAL INTELLIGENCE AGENCY

INFORMATION REPORT

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COUNTRY Switzerland

SUBJECT Pharmacology of Lysergic Acid Diethylamide (LSD-25)

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Figures referred to in text below are available on loan from CIA Library.

1. This report comprises two major parts: The first part deals with studies of LSD on the cardiovascular system with particular referen to its effects on blood pressure and its modification of responses to splanchnic, vagal stimulation and to the administration of epinephrine. The second part deals with the pyretic effects of lysergic acid diethylamide in rabbits.

BLOOD PRESSURE EFFECTS.

2. Cats anesthetized with 40 to 50 milligrams of chloralose per kilogram were used in these experiments. Ether was used as an induction anesthetic for the chloralose. The ether anesthesia lasted from five to ten minutes.

3. Blood pressure was recorded by means of a mercury manometer from the carotid artery.

4. Spinal cats were prepared under ether anesthesia by first tying the two carotid arteries, then compressing the vertebral arteries against the spinal column by a special clamp after which the animal was decapitated above the clamp. Artificial respiration was maintained in these spinal animals by means of a Palmer pump.

5. All drugs were given by means of a cannula placed in the femoral vein. The cannula was attached to a reservoir of physiological saline solution and the proper amount of drug in solution was administered through the rubber tubing to the cannula.

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6. Stimulation of the vagus and splanchnic nerves was carried out by means of a Grass stimulator. The frequency was 20 per second at four to eight volts. In each animal the stimulating voltage was submaximal.

Experimental Results.

7. General Effect on Blood Pressure. In six cats LSD was administered in doses of 100 gamma per kilogram. In three of the experiments the blood pressure fell to half to two thirds of its control level. This fall lasted from 10 to 20 minutes. In three of the cats the blood pressure showed an erratic response lasting about a minute but did not fall. In each case the dose of 100 gamma of LSD was repeated between one to two hours after the administration of the initial dose. In every case the blood pressure response to the second dose was a marked fall lasting between five and 15 minutes.

8. In spinal cats the administration of 100 gamma of LSD per kilogram did not produce any change in blood pressure.

9. On the basis of the differing response between intact chloralose anesthetized cats and spinal cats it is possible to tentatively ascribe the depressor effect of LSD to a central action.

10. Effect of Splanchnic Stimulation After LSD Administration. Approximately ten minutes after the administration of the initial dose of LSD the splanchnic nerve on the left side was stimulated with submaximal levels. The result in rise in blood pressure was compared to that produced by an equivalent level of stimulation before the administration of the LSD. The results shown in Figures one and two were from cats anesthetized with chloralose and Figure three from a spinal cat.

11. As seen in Figure one the effect of splanchnic stimulation is increased after the administration of LSD. However, in Figure two where there was no marked fall in blood pressure seen and in Figure three which is from a spinal animal there was no significant augmentation of the effects of splanchnic nerve stimulation.

12. Effect of Epinephrine Administration After the Administration of LSD. After the development of the effect of LSD on the blood pressure epinephrine was administered in doses of 2.5 gamma per kg and the effect compared with the administration of a similar dose given during the control period before the administration of LSD. In cats where the LSD produced a fall in blood pressure the effect of epinephrine was markedly increased both in the pressor response and the duration of the response. In cats where the LSD produced no marked and sustained fall in blood pressure and in the spinal animals, the epinephrine response was almost identical with that produced during the control period.

13. Effect of Vagal Stimulation After the Administration of LSD. In different animals the vagus nerve was stimulated under the following conditions: The right vagus was sectioned with the left vagus intact and the peripheral section of the right vagus stimulated; both vagi were sectioned and the peripheral sections of both the right and left vagus were stimulated. No difference was seen in the blood pressure response to vagus stimulation after the administration of LSD as compared to the results before administration.

Summary.

14. There is a differing response after the administration of LSD in chloralose anesthetized cats and in spinal cats. In the anesthetized cats the blood pressure falls while in the spinal cats it does not. There is some unreliability about the fall with the initial administration of a dose of 100 gamma

of LSD per kilogram. In some cases this fall is absent but in all cases a fall was evident after the administration of a second dose of LSD. This failure of the initial dose to produce a fall may be because in these animals the dose was inadequate.

15. It is evident that the effect of LSD on blood pressure is a central action since it is abolished in spinal animals. The augmented response to both splanchnic stimulation and epinephrine administration after LSD would apparently indicate that the LSD sensitizes the animal to these two conditions. However, this augmentation was never observed except where blood pressure was relatively low. It is likely that this augmentation of effect is not a real one; or, at least, the potentiation can be demonstrated only by more precise experimental techniques.

PYRETIC EFFECTS OF LSD IN RABBITS.

16. In observing the effects of LSD in intact rabbits it was noted that hyperpnea had developed which led to a consideration of the possibility of a pyretic action of LSD. Preliminary observations by rectal thermometer indicated that a pyretic effect did indeed exist. Examination of literature references showed no previous observation of this action in any of the animals or humans studied. Our own observations in cats showed no pyretic effects.

Experimental Methods.

17. Unanesthetized rabbits were used. Temperature was measured by means of a rectal thermometer and by means of a Dermalor applied to the skin of the abdomen and to the ear. A dose of LSD, 50 gamma per kilogram was administered intravenously or a dose of 60 gamma per kilogram administered subcutaneously. In either case the results were approximately identical.

18. Results of these experiments are seen in Figure four. The most marked effect is seen in the change in rectal temperature which rises from approximately 40 degrees centigrade to 41.5 and lasted approximately eight hours. A control rabbit receiving saline showed no such rise in rectal temperature. The ear temperature fell markedly as indicated also in Figure four whereas the ear temperature of a control animal showed no significant change. The skin temperature did not show any marked differences from that of a control.

Summary.

19. The pyretic effects of LSD stand at this point as a simple but significant observation. It is possible that the marked fall in the ear temperature is the result of constriction of the arterial supply to the ear and that the rise in body temperature is likewise due to vascular effects. It is possible that the pyretic effects of LSD are seen only in the rabbit since the rabbit ear represents a biological radiation mechanism for the maintenance of the body temperature of that species. Hence, comparable vascular effects might produce no significant temperature changes in other species.

/Available on loan from CIA Library are figures referred to in text above, as follows:

Figure 1: Reaction graphs of cat anesthetized with 40 mgm/kgm choralose.

Figure 2: Reaction graphs of cat anesthetized with 40 mgm/Kg choralose.

Figure 3: Spinal cat. Graphs showing effect of splanchnic stimulation and epinephrine injection before and after LSD.

Figure 4: Graphs representing the effects of LSD on the skin, ear and rectal temperatures in the conscious rabbit./

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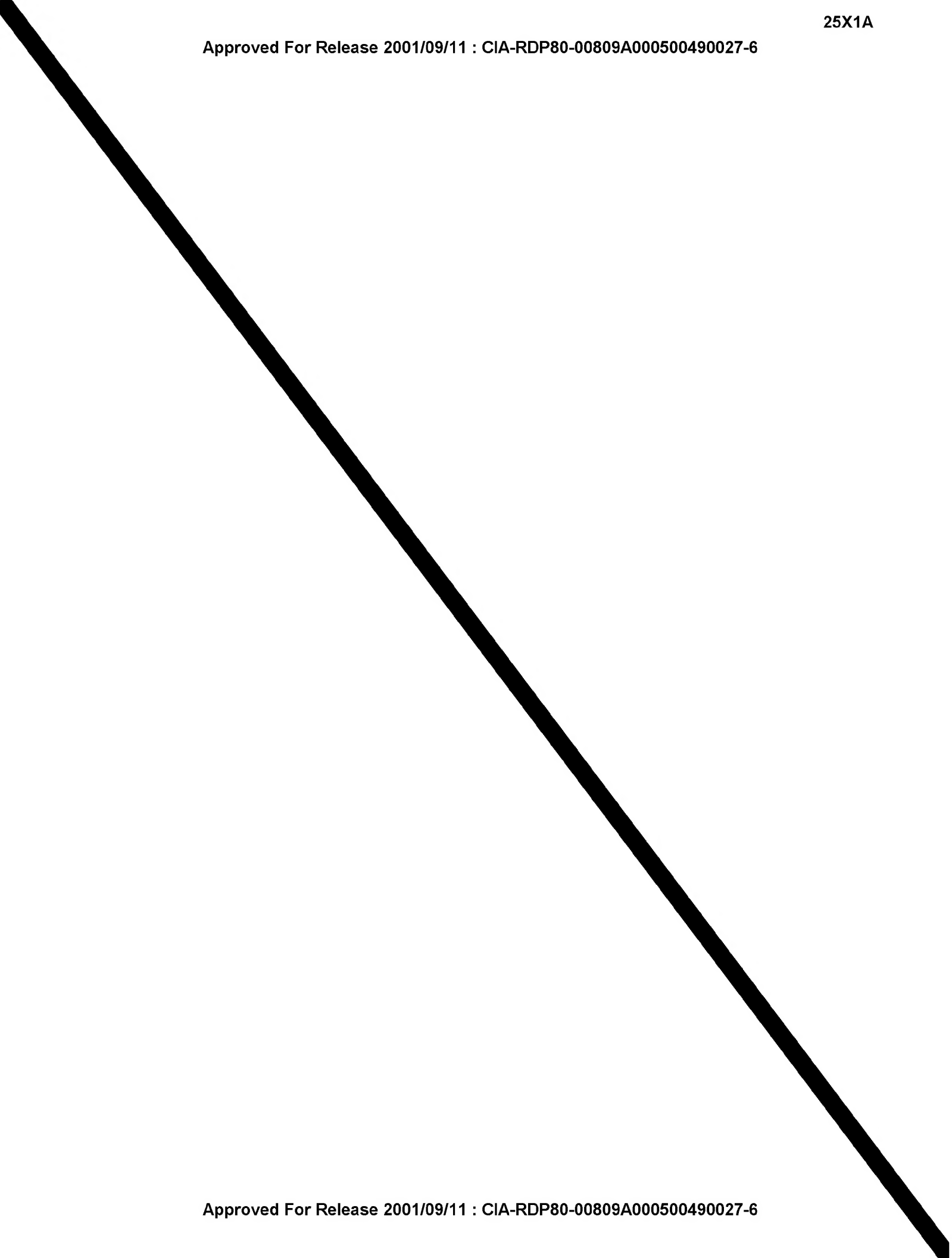

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